



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁵ : A61K 35/78, A01N 65/00</p>	<p>A1</p>	<p>(11) International Publication Number: WO 91/05561 (43) International Publication Date: 2 May 1991 (02.05.91)</p>
<p>(21) International Application Number: PCT/AU90/00487 (22) International Filing Date: 10 October 1990 (10.10.90) (30) Priority data: PJ 6773 10 October 1989 (10.10.89) AU (71)(72) Applicant and Inventor: HULL, Peter, Hugh [AU/AU]; 6 Phaff Street, Proserpine, QLD 4800 (AU). (74) Agent: PETER MAXWELL & ASSOCIATES; G.P.O. Box 3125, Brisbane, QLD 4001 (AU). (81) Designated States: AT, AT (European patent), AU, BB, BE (European patent), BF (OAPI patent), BG, BJ (OAPI patent), BR, CA, CF (OAPI patent), CG (OAPI patent), CH, CH (European patent), CM (OAPI patent), DE, DE (European patent), DK, DK (European patent), ES, ES (European patent), FI, FR (European patent), GA (OAPI patent), GB, GB (European patent), GR (European patent), HU, IT (European patent), JP, KP, KR, LK, LU, LU (European patent), MC, MG, ML (OAPI patent), MR (OAPI patent), MW, NL, NL (European patent), NO, RO, SD, SE, SE (European patent), SN (OAPI patent), SU, TD (OAPI patent), TG (OAPI patent), US.</p>		<p>Published With international search report.</p> <p>COURTESY COPY</p>
<p>(54) Title: HEAD LICE TREATMENT</p>		
<p>(57) Abstract</p> <p>There is provided a novel composition containing neem extract to repel and/or treat head lice in humans. The composition can be regularly applied to the hair and scalp of a human without being greasy and with its presence being generally understated by other humans. The composition broadly comprises a solution of azadirachtin including up to about 1 % of azadirachtin and the balance substantially all solvent suitable for permitting application of the solution to the human head. The solution may include at least 80 % of an alcoholic or spirit solvent, but non-alcoholic solvents may be used to provide a suitable vehicle to deliver the neem extract to the head preferably by means of spraying. The solvent must be able to dissolve the neem extract to produce a fine mist when sprayed and it must be acceptable to use on a human scalp.</p>		

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- 1 -

HEAD LICE TREATMENTTECHNICAL FIELD

THIS INVENTION relates to a treatment composition for humans, and it relates particularly to a novel composition containing neem extract to repel and/or treat head lice in humans.

BACKGROUND ART

Neem trees - *Azadirachta indica* - are known to grow in many countries around the world, including Kenya, Mauritius, India, Thailand, Indonesia and Australia. There may be slight variations in trees from one location to another, but they all have one thing in common - they all produce a naturally occurring insecticide called azadirachtin. Most of the azadirachtin is produced in the seeds of the tree, although some is contained in the bark and leaves. Whilst neem seed extract is used as an insecticide and repellent in farm animals, its application to humans has not been fully explored. In Australian Patent Application No. 26320/88, reference is made to application of azadirachtin to humans. However, the azadirachtin is applied to humans as an ointment for the hair and scalp. Ointments are generally not acceptable to users who do not wish to have them in their hair for abnormally long periods of time.

Accordingly, investigations were carried out with the principal object of developing a composition which could be regularly applied to the hair and scalp of a human, not be greasy and its presence being generally understated by other humans. To have the best possible chance of success, the composition should be capable of being sprayed directly onto the scalp using a volatile solvent that would not be an irritant to the scalp and would evaporate away, leaving the active ingredient behind to do its intended job. The criteria selected for success were that the composition should be -

1. acceptable for the human to wear as a preventative virtually 24 hours a day;

- 2 -

2. capable of easy and convenient application to use;
3. a successful repellent, and
4. unable to damage the hair as present lice treatments can do.

5 Initially traditional repellents were investigated such as eucalyptus oil, citronella oil and similar products, to compare them with azadirachtin. However, it was quickly established that these were unacceptable for application to hair due to either their offensive smell or
10 potential toxicity to humans. Whilst neem has an offensive odour, it is effective in such low concentrations that it is easy to hide the offending smell using natural fragrances such as a mixture of green apple and lemon.

DISCLOSURE OF THE INVENTION

15 In one preferred aspect of the invention, a composition is provided comprising a solution of azadirachtin including up to about 1% of azadirachtin and the balance substantially all solvent suitable for permitting application of the solution to the human head.
20 Preferably the solution includes at least 80% of an alcoholic or spirit solvent.

This solution has, in testing, been found to be an excellent treatment and repellent of head lice in humans. More particularly, typically when acting as a treatment,
25 azadirachtin is present in amounts of about 200-2000 parts per million (ppm). Whilst acting as a repellent, azadirachtin is typically present in amounts of 10-1000 ppm.

Any solvent that lends itself to providing a suitable
30 vehicle to deliver the neem extract to the head by means of spraying would be acceptable in the formula, the solvent properties required being that it must dissolve the neem extract, must produce a fine mist when sprayed, and must be acceptable to use on a human scalp.

35 Typically alcohols are suitable solvents. The type of alcohol used may be of any variety such as isopropyl alcohol or ethyl alcohol.

- 3 -

Other additives may be in the solution, such as perfumes, conditioners and colours, as referred to hereinafter.

As an illustrative example of the composition for sale as a chemist's line, the solution may comprise neem seed extract (5%) to 1.00 parts and mixed fruit perfume to 0.5 parts, the balance to 100 parts being industrial methylated spirits.

BEST MODE FOR CARRYING OUT THE INVENTION

The invention is now described with reference to the following trials. An important fact in such trials was "Patient Compliance". It is very important that the patient complies with the instructions and if the instructions are not followed, false results will occur.

The repellent was sprayed onto two places on the scalp of a number of participants in the trials, on two mornings a week, Monday and Wednesday.

The application of the spray was carried out only after the hair and scalp had been thoroughly dried should the participant have washed or wet his/her head. The hair was parted to expose the scalp and the repellent sprayed onto the scalp itself. One spray was applied to the front of the head, and one to the back of the head, and massaged into the scalp. The participants were advised that washing of the hair washed out the active ingredient.

The tests were designed to establish:

1. whether the participants would take the trouble to apply the spray as directed;
2. whether the participant would be happy to wear the product, and
3. the optimum strength and frequency of application for best results. In each test case, the participants were asked to apply the product as directed, and observe reactions and results as accurately as possible.

The trial results were also assessed to establish effectiveness for two purposes: (1) to kill and eradicate

- 4 -

the lice, and (2) to repel lice and thereby avoid further re-infestation.

In some of the trials, ethyl alcohol was used as the carrier solvent for several reasons -

- 5 (a) It is an effective solvent of azadirachtin;
- (b) It is non-toxic to humans when applied to the skin;
- (c) It evaporates quickly, leaving the active ingredient behind on the hair and scalp, and
- 10 (d) It lends itself to easy and effective vaporisation when used in a non-aerosol pump spray.

As there is a proportion of any population who have dry hair, and an alcoholic spray may exacerbate the dry hair condition, it was decided to also conduct similar tests using light liquid paraffin as a carrier solvent.

- 15 When preparing the test solutions, a perfume was added comprising equal parts of green apple and lemon fragrances, and the fragrance of the composition was found acceptable to all the participants.

- 20 Test solutions was made containing various strengths of azadirachtin content. Strengths used varied from 200 parts per million (ppm) to 1000 ppm of azadirachtin. Solvents used were light liquid paraffin and 90% ethyl alcohol. It was found that as soon as water was added to the alcoholic solution, the azadirachtin started to "throw out" of solution. Any dilution of the alcohol base below 80% alcohol content rendered it useless as a solvent for azadirachtin. A simple pump top spray bottle was used to deliver the product to the scalp.

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- 30 Eleven participants were tested and given a set of printed instructions.

Results

Participant 1

- 35 The test solution was spirit based containing 800 ppm azadirachtin. From day 1 the test repelled lice. Whereas in the past, the participant was susceptible to be re-infested every three or four weeks, the participant became lice free for the term of the test (approximately three

- 5 -

months) notwithstanding being exposed to lice. The participant's parents reported that the participant's hair condition had improved as well. The participant was happy to use the composition.

5 Participant 2

The solution supplied was paraffin oil based, with 500ppm of azadirachtin. The participant reported results consistent with the experiences of Participant 1.

Participant 3

10 The solution was spirit based and contained 500 ppm of azadirachtin. The participant reported results consistent with the experiences of Participant 1.

Participant 4

15 The solution was spirit based and contained 500 ppm of azadirachtin. From day 1, lice infestation was inhibited and the participant was happy to wear it. Again hair condition improved.

Participants 5 and 6

20 The solution was spirit based and contained 400 ppm of azadirachtin. Participants 5 and 6 were from the same family and lived in the same household. Both reported results consistent with the experiences of Participant 1.

Participant 7

25 The solution was spirit based and contained 600 ppm of azadirachtin. Again the results indicated the solution maintained Participant 7 lice free over the test period compared to consistent lice problems in the last few years.

Participant 8 - was a family.

30 This household was made up of two women, each with two children, living together, with a never ending problem of head lice infestation. One of the women and her children had very thick wavy long hair, which is very difficult to treat. In view of the number of persons in the house, there was always someone in the house with lead lice.
35 Further the woman and child with wavy hair also had oily hair and so were treated with a spirit based composition containing 400 ppm of azadirachtin in 90% ethyl alcohol.

- 6 -

The other woman and her children had dry hair, and so were treated with an oil based composition containing 400 ppm in light liquid paraffin. For the first two weeks no lice were evident. However, subsequently one of the daughter's hair was heavily infested. That child had very thick wavy long oily hair, which was so curly that the parent has never been able to totally eradicate the lice and eggs. Consequently, treatment was carried out with a stronger solution being spirit based containing 1000 ppm of azadirachtin with instructions to use it as a treatment rather than a repellant. The daughter was told to spray it all over the head rather than in just two spots, to ensure that the whole head, scalp and hair were covered by the treatment. Within two weeks the daughter was completely free from any infestation for the first time. Further her hair was also looking better than it had ever looked, apparently as a result of the treatment. All in the household were then free of infestation and commented that all their hair was looking better than ever.

20 Participant 9

The solution was spirit based containing 500 ppm of azadirachtin. No lice were evident from day 1 for the duration of the test period (three months). The participant reported consistently with Participant 1.

25 Participant 10

The solution was spirit based containing 200 ppm of azadirachtin. This was by far the lowest strength solution tested and was used to try to eradicate the lice. It failed to achieve this within seven days. Once lice were eradicated, the solution was again applied according to the testing procedure. Participant 10 reported no more lice problems.

Participant 11

The solution was spirit based containing 500 ppm azadirachtin. Early reports were very enthusiastic and the hair condition had improved. However, after four weeks Participant 11 reported a severe outbreak, with mobile lice

- 7 -

and eggs aplenty. The participant had found them on the Saturday, so had immediately treated them with Lindane. He was supplied with the new high strength test solution which was spirit based, 1000 ppm of azadirachtin, with
5 instructions to use it to ensure complete eradication of the lice and eggs, then to stay on the higher strength as a bi-weekly repellant. Results were completely satisfactory, the higher strength eradicated the problem and the repellant was effective.

10 The formulae used in the trials used ethyl alcohol 90% and light liquid paraffin. The light liquid paraffin was only given to two participants to try, as it was considered to be likely to be less successful than the spirit base due to its oiliness on the scalp and less effective
15 vaporisation when sprayed from a pump spray. Of the two participants supplied with the oil based test samples, only one persisted with it. That participant, however, reported complete success.

As indicated previously, the ethyl alcohol used as the
20 spirit base needs to be at least 80% alcohol content. Other alcohols such as isopropyl alcohol may be suitable as a solvent base to deliver the azadirachtin to the scalp. Perfume may be added to hide the rather offensive smell of the neem extract, but since the neem extract is required in
25 such low concentrations, it is not difficult to hide the smell.

It would appear from the testing programme that the solution is easily dispersed in a pump top spray, which makes the product easy to use for the parents and is
30 readily acceptable by the children. Aerosol spray application would have equal acceptance. The important aspect of the invention is that the solution allows the neem extract to be delivered directly to the hair and scalp by a solvent that thereafter evaporates away, leaving the
35 active ingredient - the neem extract.

In summary, the solution according to the invention is effective as both a repellant and a treatment for the

- 8 -

5 killing and eradicating of head lice and their eggs from
the human head. Any perfume that hides the bad smell of
the neem extract would be acceptable. One unexpected
additional advantage of use of the neem extract is
apparently its effect as a hair conditioner, so it would
not be necessary to add extra conditioners to the
formula, such as lanoline, in order to condition the hair.

10 Although the neem extract on its own has proven to be
completely effective for the purposes outlined above, it is
extremely expensive. Accordingly, it is also envisaged
that activity enhancers, such as pyrethrums, may be added
to the formula in order that the strength of the neem
extract may be reduced without detracting from the efficacy
of the product.

15 The various examples described have been given by way
of illustrative example only and various changes and
modifications may be made thereto without departing from
the scope and ambit of the present invention as defined in
the appended claims.

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- 9 -

CLAIMS

1. A composition for use in repelling and/or treating head lice in humans, comprising a solution of azadirachtin including up to about 1% of azadirachtin, and the balance substantially all solvent suitable for permitting application of the solution to the human head.
2. A composition for use in repelling and/or treating head lice in humans, comprising a solution of azadirachtin including up to about 1% of azadirachtin and at least 80% of an alcoholic or spirit solvent.
3. A composition for use in treating head lice in humans, comprising a solution of azadirachtin including about 200-2000 parts per million (ppm) of azadirachtin and at least 80% of an alcoholic or spirit solvent.
4. A composition for use in repelling head lice in humans, comprising a solution of azadirachtin including about 10-1000 parts per million (ppm) of azadirachtin and at least 80% of an alcoholic or spirit solvent.
5. A composition according to any one of the preceding claims, wherein the solvent has properties permitting achievement of a fine sprayed mist of the solution of azadirachtin.
6. A composition according to any one of the preceding claims, wherein the solvent is isopropyl alcohol or ethyl alcohol or other equivalent alcoholic solvent.
7. A composition according to Claim 1 wherein the solvent is paraffin or equivalent non-alcoholic solvent.
8. A composition according to any one of the preceding claims, wherein the solution includes natural fragrances or perfumes to mask undesirable odours.
9. A composition according to Claim 8 wherein the perfume is selected from a group including green apple and lemon fragrances and mixed fruit perfume.
10. A composition according to any one of Claims 2 to 5 wherein the solution comprises 1.0 parts of neem seed

- 10 -

extract (5%), together with 0.5 parts perfume, and the balance to 100 parts being industrial methylated spirits constituting the solvent.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/AU 90/00487

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) 6		
According to International Patent Classification (IPC) or to both National Classification and IPC		
Int. Cl. ⁵ A61K 35/78; A01N 65/00		
II. FIELDS SEARCHED		
Minimum Documentation Searched 7		
Classification System	Classification Symbols	
IPC	A61K KEYWORD: AZADIRACETIN	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched 8		
III. DOCUMENTS CONSIDERED TO BE RELEVANT 9		
Category*	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages 12	Relevant to Claim No 13
P,X	US,A, 4946681 (WALTER) 7 August 1990 (07.08.90)	(1-6)
Y	US,A, 4556562 (LARSON) 3 December 1985 (03.12.85)	(1-6)
X	AU,A, 11220/88 (GUERRINI, V.H.) 19 January 1989 (19.01.89)	(7)
X	AU,A, 26320/88 (UNIVERSITY OF QUEENSLAND) 1 June 1989 (01.06.89)	(7)
<p>* Special categories of cited documents: 10</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"Z" document member of the same patent family</p>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search 5 December 1990 (05.12.90)	Date of Mailing of this International Search Report 21 December 1990	
International Searching Authority Australian Patent Office	Signature of Authorized Officer J.P. PULVIRENTI	

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON
INTERNATIONAL APPLICATION NO. PCT/AU 90/00487

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Members
US 4946681	US 4946681	
US 4556562	US 4556562	
AU 26320/88	AU 26320/88	
AU 11220/88	AU 11220/88	

END OF ANNEX

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